THE SUMMER'S EXPERIENCE WITH INFECTIOUS DIARRHŒA

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THE presentation of this paper viz.: "A Summer's Experience with Infectious Diarrhœa," was prompted by a desire to present to the medical profession in general, in Toronto, and to the pediatrists in particular, some aspects of a disease which has been of considerable interest to myself and more or less of a puzzle in so far as its management and treatment was concerned.

Its greater prevalence in the city this year as compared with previous years has been remarked upon by several of you, and it has, therefore, become of more immediate interest.

In this contribution, you will find no attempt at original investigation, but merely a résumé and impartial criticism of the work done during the summer, in the hope of deriving from a rather hopeless confusion of figures some helpful hints as to the diagnosis, prognosis, pathology and treatment of infectious diarrhœa in early life. Owing to the fact that the decision to report these cases was not made until the last but one had been discharged from observation, the records are not as complete as I would have liked; for example, the failure in several instances to confirm bacteriologically the clinical diagnosis.

Infectious diarrhœa is, as its name implies, a bacterial infection of the mucous membrane of the small and large intestine, usually the ileum and colon caused by the ingestion of various organisms such as B. dysenteriæ, streptococcus, B. coli, and Welch bacillus, or by the lighting into pathological activity of one of the organisms normally present in the digestive tract. This infection manifests itself clinically by a diarrhœa characterized by frequent painful evacuations of the bowels, containing pus, mucus and blood, and by a toxæmia, as evidenced by pyrexia and prostration. Clinically, the diarrhœa caused by the various organisms is identical, varying only in severity, and it is impossible always to separate cases of

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fermentative diarrhœa from those caused by bacterial infection, without bacteriological aid.

The difficulty in classification is due not to the fact that fermentative diarrhœa may simulate infectious diarrhœa, but to the fact that mild cases of dysentery may pass unrecognized owing to the absence of pus or blood in the stools. It is these mild unrecognized cases which are, not improbably, responsible for the spread of the infection when it is seen in the epidemic form.

In the series of cases presented, eight were proven bacteriologically or serologically to be cases of true dysentery. In three others the only gram-negative bacillus isolated was B. coli. In none was the infecting organism proven to be a streptococcus or B. Welchi. There were in all eighteen cases, and a brief summary of their records from an ætiological, clinical and pathological standpoint, reveals a few facts of interest.

Ætiology. An effort was made to discover an adequate explanation for the increased prevalence of the disease in the city during the past summer, and also a clue as to a common source of infection for all the cases. The increased incidence noted recently of communicable diseases, such as purulent gingivitis (or trench mouth) and venereal disease, due to return from overseas of infected men prompted the assumption that the much maligned returned man was responsible for the increase of dysentery.

Investigations along this line were, however, unsatisfactory and unconvincing. Surprisingly few cases had, previous to the onset, been in contact with returned soldiers and in no instance was a direct contact with a convalescent dysentery case proven. When, however, one considers the chief methods of transmission of infection of this disease it becomes obvious that personal contact plays only a very small part, and I am still convinced that the most rational explanation is the presence in the community of returned soldier dysentery carriers.

Zinsser[1] and Smillie[2] have separately shown the possibility of transmission by food stuffs, and Lucas and Amoss[3] during an epidemic of infectious diarrhœa actually caught the flies red-handed with viable dysentery bacilli on their bodies. The majority of observers are agreed that the common house-fly is the most frequent cause of the spread of the infection basing their belief on the continued prevalence of the condition during the later summer months, when the heat is not excessive but flies are still numerous. In this series, eleven cases occurred in July, four in August, and four in September.

From a study of records kindly furnished me at the Meteorological Office, it appears that 55 per cent. of the cases occurred during the months having the highest average maximum temperature, 85°, the highest monthly mean temperature, 73°, and the lowest mean humidity 68°. This was July.

An attempt was made to establish a common source of food supply in these cases, but with no result. In one house, for instance, where four cases occurred, it was impossible to find even one article of diet which was common to all four. Three cases gave a history of having eaten ice-cream cones, two or three days previous to the onset, and three others had eaten fresh fruit procured from the local fruit shop. Both these food stuffs have been shown by other observers to be the medium of transmission of infection. No grouping of the cases into one locality or nests of infection could be demonstrated, the infected houses being scattered indiscriminately throughout the city, only two being on the same street. It is interesting that in nine instances there were two or more cases in the same house.

Age incidence. Only five were under one year, four between one and two; five between two and three, and five over three years. The small percentage of infants explains the comparatively low mortality for the series, viz.: 31·6 per cent.

Symptoms. The onset was abrupt in 90 per cent. and was characterized by vomiting in 60 per cent.; diarrhœa, 100 per cent.; blood in stools, 80 per cent.; convulsions 20 per cent. The history relating to pus in the stools, fever, and tenesmus was too indefinite to be worth recording. Whilst under observation all cases had pyrexia of greater or less degree, depending on the severity of the infection. It has been shown by other observers that the prognosis can be based in some measure on the height of the temperature, and the rule held good in this series. Four cases in which the maximum temperature was 101° or less, recovered. In five cases where the temperature rose to 103° the mortality was 20 per cent.; and of nine patients whose temperature registered over 103°, 55 per cent. died. For the purpose of comparing the mortality of fermentative diarrhœa with the infectious form, eighty-two consecutive cases of the former type admitted to the wards of the Hospital for Sick Children, during July and August, were tabulated. The mortality was found to be 43 per cent., but it should be noted that the average age of these patients was much below the average in the series of infectious diarrhœa. The same relationship between the height of the fever and the mortality does not exist to the same

extent in the Fermentative group. Vomiting during the course of the disease was present in 30 per cent., but was excessive in only 16 per cent. The spleen was slightly enlarged in 10 per cent. As an aid in diagnosis, the blood count is of questionable value. All the blood examinations in this series were made in the first week of the disease. The lowest total count was 7,600 per c.mm., the highest 18,600; the polymorphonuclear percentage ranging from 37 to 71. The average total count of uncomplicated cases was 10,000, and average polymorphonuclear percentage 59. These figures tally with those obtained by Bloom[4].

Blood cultures were made in three cases, and, as was to be expected, were sterile. The invasion of the blood stream by dysentery organisms has been reported by several investigators, but it is a very unusual occurrence.

Stools. The character of the stools is typical of the condition. During the first three or four days there are numerous evacuations containing blood, and clear or slightly turbid mucus, with little fæcal material, and accompanied by tenesmus. After this period the mucus changes to pus, and fæcal matter begins to appear. The reaction is usually alkaline to litmus. In eight cases tested in this collection, only one stool was acid to litmus.

I should like to emphasize here that the direct smear of the stool stained by Gram's method is very typical of the disease, and where conditions do not permit a culture being made, a fairly accurate diagnosis can be achieved by the clinical signs, reaction of the stools, and a study of the direct smear. Numerous pus cells are seen with very few organisms, the latter being mainly Gram-negative bacilli, a few streptococci and occasionally Gram-positive bacilli.

Bacteriology. In spite of the enormous amount of work done to determine the bacteriology of infectious diarrhœa, the results obtained have been conflicting. In this country, the most thorough investigation was done by Kendall, Walker, and Smith of Boston[5,6,7,8]. They conclude that any one of the following organisms may be the cause of dysentery or infectious diarrhœa: (1) B. dysenteriæ of Flexner; (2) The Shiga type; (3) B. ærogenous capsulatus or Welch bacillus; (4) B. coli and (5) streptococcus. Their deductions are based on the isolation of any one of these organisms from the stools. Since, however, B. coli, streptococcus and the Welch bacillus are frequently found in the dejecta of normal bottle-fed infants, or children on a mixed diet, the preponderance of one of these organisms in a diarrhœa stool does not *per se* justify the conclusion that

it is the exciting cause of the diarrhœa. The performance of serological tests, such as agglutination reactions or complement fixation tests would have materially strengthened their position. There is, however, a diversity of opinion as to what dilution of serum giving a positive reaction should be considered as being within the normal limits, two observers placing the diagnostic limit for the Flexner organism at 1-250.

Dr. Graham, Professor of Department of Medicine, who has done a great deal of work along this line, while attached to the Salonica Forces, summed up the opinion prevailing at present in a recent personal communication. Firstly, failure to isolate B. dysenteriæ from stools even after repeated attempts does not mean that this infection can be ruled out. After the first week of the disease, when stools contain fæcal material, it becomes increasingly difficult to obtain the dysentery bacillus by the ordinary culture methods. It is this well recognized difficulty which tends to throw doubt on the work of those observers who report diarrhœas caused by such organisms as Gaertner's bacillus, Morgan's bacillus, or B. ærogenous capsulatus. Secondly, failure to demonstrate specific agglutinins in the blood serum is not a final test, since the intensity of the reaction depends entirely on the strain used. Thus a strain, the titre of which has been worked out by personal experience gives the most uniform results.

Agglutination tests were done in eight cases in this series, using both a Shiga and Flexner strain. Five showed reactions which were of diagnostic significance; two of them agglutinating the Flexner organisms in dilutions of 1-160 or higher, one at 1-80, and one agglutinated the Shiga bacillus at a dilution of 1-640.

There was a certain amount of co-agglutination between the two strains. To obtain a standard for these two agglutinogens, the blood of ten normal children was tested. In only two instances did a reaction occur in dilutions higher than 1-20, and none higher than 1-40.

Pathology. Three cases came to autopsy, and two of them showed fairly typical lesions. None of the three cases had been proven bacteriologically or serologically to be dysentery.

Case 4 showed a broncho-pneumonia, acute glomerular nephritis, pseudomembranous enteritis, and superficial ulceration in ileum and colon.

Case 6. A broncho-pneumonia was found, and, to quote the autopsy records written by Dr. Erb, attending pathologist to the hospital: "The mucous membrane of the lower three feet of ileum,

and the whole of the colon is covered with a yellowish pseudo-membrane which on removal reveals a granular reddened surface, which appears to be ulcerating. The membrane is removed with considerable difficulty. Solitary follicles and Peyer's patches not enlarged. Mesenteric lymph nodes pale and much enlarged.

Case 7 showed an acute nephritis, broncho-pneumonia, and, in the last foot of the ileum and the whole of the colon, scattered areas of inflammation of mucous membrane."

Treatment. As far as concerns the management of infectious diarrhœa in infants, there are two distinct schools of teaching on this continent. Their views are so diametrically opposed that it seems improbable that both can be right. The Boston school bases its treatment viz.: the exhibition of lactose, on certain fundamental biochemical and bacteriological principles. The opposing school bases its treatment, viz.: administration of protein milk, on no sound theoretical principles, but merely on the assumption that if protein milk is of value in most cases of diarrhœa, it ought to prove of value in all of them. The work done by Kendall in Boston is convincing and very instructive, and I will endeavour to give you an outline of it as compactly and comprehensively as possible.

1. During a period of starvation, sugar which has been stored up in the liver in the form of glycogen is rapidly exhausted. When it is finished, protein metabolism commences. This sugar, therefore, acts as a protein sparer.

2. It can be readily shown by a simple laboratory experiment that members of a certain group of bacteria, amongst them being B. dysenteriæ, if inoculated into media containing both a protein substance and a fermentable carbohydrate, will attack the carbohydrate first, and when this is finished, but not before, will attack the protein, break it down, and liberate toxic products of putrefaction. In other words, fermentation takes precedence over putrefaction when both carbohydrate and protein are present in the media in which the organism is growing.

3. The specific toxin of the bacterium is produced, most readily in an alkaline medium containing protein.

4. Formation of lactic acid, as one of the end products of fermentation tends to inhibit the growth of the B. dysenteriæ and streptococcus.

Adopting these known facts as a basis for treatment the patients were furnished with a solution of an easily assimilable, readily fermentable carbohydrate, viz.: lactose, with the belief

that the patient would be benefitted in three ways (1) By a diminished absorption of the products of protein decomposition; (2) By the ingestion of a readily assimilable food; (3) By the inhibition of the growth of the putrefactive organisms and of the formation of specific bacterial toxines, as a result of the production of lactic acid.

Theoretically the treatment is sound and practically it has stood the test, judging from the results published by Kendall, Bowditch[9], Morse[10], and others.

After reviewing the work and conclusions of these observers, it is very difficult to justify the use of protein milk in the treatment of this disease, and I believe that we have been, to say the least, ultra-conservative in that we have not even given the above treatment a fair trial.

In this series, eighteen cases were fed protein milk as soon as they came under observation and were kept on it for a period varying from one to forty days. The other case was given boiled skimmed milk and decided improvement in the character of the stools was noted in eight days. This was an exceptionally mild case of proven dysentery in an older child, the temperature never rising about 100°. With several of the patients the protein milk was temporarily discontinued and other foods such as skimmed milk, junket, and cereals, etc., were tried with no apparent change in frequency or character of the stools. Colon irrigations were given in four instances without obvious beneficial effect. Repeated injections of normal saline or 5 per cent. glucose solutions were administered, hypodermically, intravenously or intraperitoneally in twelve cases in which dehydration had to be contended with. The value of this procedure was not sufficiently emphasized by the Boston school, but it is unquestionable.

Specific antitoxine therapy was not employed in any instance, as it was found impossible to procure the serum, but good results are reported with its use.

The literature contains many reports of the successful use of autogenous vaccines and when the antitoxic serum is not available, they should be tried.

It is impossible to go into each case in this series, in detail, but the clinical histories of one or two are instructive.

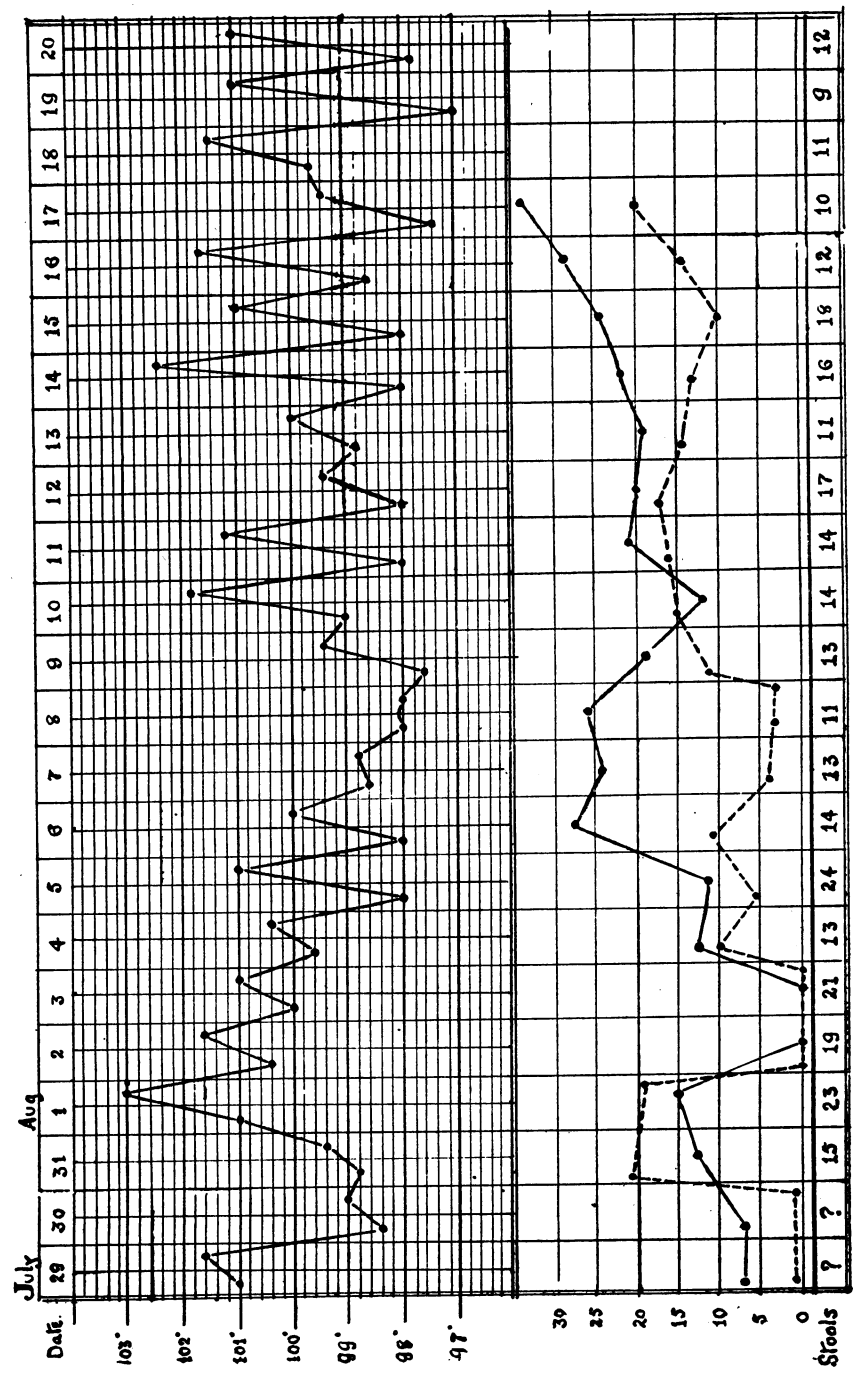
Case 1. Male, age five months, was given protein milk mixture, half-strength, on admission. His temperature was then 98°, but rose in two days to 104°, when death occurred, ushered in by meningeal signs suggesting a profound toxæmia. The examination of the spinal fluid was negative.

Case 2. Male, age five years. Given on admission full strength protein milk, and twenty-four hours later barley gruel which was kept up for another five days. His temperature on admission was 100°, but reached normal on the eighth day. The stools decreased from sixteen to five per diem in four days whilst on barley gruel.

Case 3. Female of nine months was given protein milk twelve hours after admission, and this food was not changed for thirty-nine days. For twenty-two days her temperature fluctuated between 99° and 103° and stools averaged five per diem. She ultimately recovered.

Case 19. Female, age six months, is still under observation. Protein milk two-thirds was given on admission, and child was on this food for fourteen days; the temperature during that period fluctuating between 99° and 104°. Five per cent. lactose solution was then given by mouth and daily hypodermoclyses of glucose solution. The day following the administration of lactose the temperature dropped to 99°, and hovered around this point for four days, when it suddenly rose to 102°, and then dropped to 98°, where it stayed for two days. The stools diminished in frequency for the first four days following the exhibition of lactose and a direct smear of one of them, stained by Gram's method presented a picture which is considered typical, viz.: the disappearance of the Gram-negative bacilli, and streptococci, and the reappearance of numerous Gram-positive bacilli of the B. acidophilus type. Two attempts have been made to isolate B. dysenteriae from the stools of this patient without success.

Case 17. Female, age four years, a proven case of dysentery, was sick eight weeks, the pyrexia persisting for five weeks. The food was changed many times, protein, klim, skimmed milk, barley gruel and soft diet, all being tried. The chart which I will shew is instructive in that it pictures the temperature curve of an uncomplicated case of true dysentery of unusual severity and duration. In it, I have endeavoured to shew a relation between the daily protein intake and the height of the pyrexia. The stroked line in the lower part of the chart represents the number of grams of protein ingested each day. The solid line represents the daily carbohydrate intake. It will be seen that in some measure the curve of the protein intake follows the temperature curve above; for instance, a drop in the pyrexia on July 29th and 30th when only barley water was administered, a sharp rise to 103° following feeding of protein milk on July 31st, a gradual reduction of temperature from the 1st of August to the 4th, when nothing but water was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given. From the 5th to 9th the daily intake of protein was comparatively low but the carbohydrate intake was markedly increased. It is possible that it was this carbohydrate excess which delayed or prevented the bacterial action on the protein and interfered with the formation of products of putrefaction, thus causing a reduction of the temperature. The wide fluctuations of temperature from August 10th to August 20th are suggestive of an ulcerative condition in the intestine which would facilitate the absorption of toxic products.

The indications for treatment then are (1) neutralization of specific toxines by injection of a specific antitoxine if this is available; (2) correction of dehydration by saline or glucose injections; (3) prevention of formation of toxic products of protein putrefaction by administration of a food rich in carbohydrate; (4) specific therapy.

In a small series of cases such as this it is obviously absurd to attempt to draw conclusions, but the summer's experience has left me with a definite conviction that protein milk is contraindicated in cases of infectious diarrhœa of the dysentery type, and I think this conviction is shared by other pediatrists in Toronto who have followed these cases, or similar ones. It is my hope that this report may serve to stimulate us to the formation of a more accurate bacteriological diagnosis of the disease, and to the institution of a more logical treatment based on a correct conception of the fundamental biochemical principles involved.

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